General

Guideline Title

ACR Appropriateness Criteria® abnormal vaginal bleeding.

Bibliographic Source(s)

Khati NJ, Glanc P, Bhosale PR, Harisinghani MG, Harris RD, Kim YB, Mitchell DG, Nyberg DA, Pandharipande PV, Pannu HK, Shipp TD, Siegel CL, Simpson L, Wall DJ, Wong-You-Cheong JJ, Zelop CM, Javitt MC, Expert Panel on Women's Imaging. ACR Appropriateness CriteriaÂ® abnormal vaginal bleeding [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 13 p. [63 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Bennett GL, Andreotti RF, Lee SI, Allison SO, Brown DL, Dubinsky T, Glanc P, Mitchell DG, Podrasky AE, Shipp TD, Siegel CL, Wong-You-Cheong JJ, Zelop CM, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® abnormal vaginal bleeding. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p. [59 references]

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Abnormal Vaginal Bleeding

Variant 1: Postmenopausal vaginal bleeding. First study. (Endometrial sampling may also be performed initially followed by imaging if results are inconclusive or symptoms persist despite negative findings.)

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transvaginal	9	3-D imaging may be a useful adjunct to 2-D imaging to better characterize an intracavitary abnormality.	O
US pelvis transabdominal	8		O
US saline infusion sonohysterography	6	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	5	This procedure may be useful to better characterize a focal or diffuse endometrial abnormality.	O
CT pelvis with contrast	2		☢☢☢

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	2		O
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
MRI pelvis without contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Postmenopausal vaginal bleeding, endometrium ≤5 mm by transvaginal ultrasound. (Some centers may choose to use ≤4 mm rather than ≤5mm. Please see narrative.) Follow-up study.

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transabdominal	4		O
US duplex Doppler pelvis	4	Color-flow Doppler may be useful for interrogation of a heterogeneous endometrium in searching for a focal versus diffuse abnormality.	O
US saline infusion sonohysterography	2		O
MRI pelvis without and with contrast	2		O
CT pelvis with contrast	1		☢☢☢
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
MRI pelvis without contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Postmenopausal vaginal bleeding, endometrium >5 mm by transvaginal ultrasound. (Endometrial sampling would also be warranted in this clinical setting to evaluate for malignancy.) (Some centers may choose to use >4 mm. Please see narrative.) Follow-up study.

Radiologic Procedure	Rating	Comments	RRL*
US saline infusion sonohysterography	8	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	6	This procedure may be useful to better characterize a focal or diffuse endometrial abnormality.	O
MRI pelvis without and with contrast	5	This procedure is appropriate when SIS is not feasible or there is the need to define extent of disease with endometrial cancer. See statement regarding contrast in the text below under "Anticipated Exceptions."	O
US pelvis transabdominal	4		O
MRI pelvis without contrast	2		O
CT pelvis with contrast	2		☢☢☢
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation**

Radiologic Procedure	Rating	Comments	RRL*

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Premenopausal vaginal bleeding. First study.

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transvaginal	9	3-D imaging may be a useful adjunct to 2-D imaging to better characterize an intracavitary abnormality.	O
US pelvis transabdominal	8		O
US duplex Doppler pelvis	5	This procedure may be useful to better characterize a focal or diffuse endometrial abnormality.	O
US saline infusion sonohysterography	4	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
CT pelvis with contrast	2		☢☢☢
MRI pelvis without and with contrast	2		O
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
MRI pelvis without contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Premenopausal vaginal bleeding, endometrium <16 mm by transvaginal ultrasound. Follow-up study.

Radiologic Procedure	Rating	Comments	RRL*
US saline infusion sonohysterography	6	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	6	May be useful to better characterize a focal or diffuse endometrial abnormality.	O
US pelvis transabdominal	4		O
CT pelvis with contrast	2		☢☢☢
MRI pelvis without and with contrast	2		O
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
MRI pelvis without contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: Premenopausal vaginal bleeding, endometrium ≥16 mm by transvaginal ultrasound. Follow-up study. (Endometrial sampling may also be warranted in this clinical setting depending on patient risk factors for malignancy.)

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transvaginal	9	Early to mid-proliferative	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
		phase of the menstrual cycle or following administration of progesterone.	
US saline infusion sonohysterography	7	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	5	May be useful to better characterize a focal or diffuse endometrial abnormality.	O
MRI pelvis without and with contrast	5	See statement regarding contrast in the text below under "Anticipated Exceptions."	O
US pelvis transabdominal	4	This procedure may be helpful if the uterus is in a neutral position or if uterine penetration by TVUS is poor.	O
MRI pelvis without contrast	3		O
CT pelvis with contrast	2		☢☢☢
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: Heterogeneous endometrium or suspected focal abnormality at transvaginal ultrasound. Follow-up study.

Radiologic Procedure	Rating	Comments	RRL*
US saline infusion sonohysterography	8	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	7	This procedure may be useful to better characterize a focal or diffuse endometrial abnormality and to evaluate for vascular pedicle flow or irregular vessels in endometrial cavity.	O
MRI pelvis without and with contrast	5	Consider this procedure if SIS is not feasible. See statement regarding contrast in the text below under "Anticipated Exceptions."	O
MRI pelvis without contrast	4		O
US pelvis transabdominal	4	This procedure may be helpful if the uterus is in a neutral position or if uterine penetration by TVUS is poor.	O
CT pelvis with contrast	2		☢☢☢
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: Endometrium not adequately visualized at transvaginal ultrasound. Follow-up study.

Radiologic Procedure	Rating	Comments	RRL*
US saline infusion sonohysterography	8		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transabdominal	6		O
MRI pelvis without and with contrast	6	Consider this procedure if SIS is not feasible. This procedure would be preferred if underlying malignancy is suspected. See statement regarding contrast in the text below under "Anticipated Exceptions."	O
MRI pelvis without contrast	4		O
US duplex Doppler pelvis	3		O
CT pelvis with contrast	2		☢☢☢
CT pelvis without contrast	1		☢☢☢
CT pelvis without and with contrast	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Virtually every woman will at some point in her lifetime experience episodes of vaginal bleeding that will be perceived as abnormal. From menarche to menopause, the average menstrual cycle is 29 days long, with a range of 23 to 39 days. Overall, the length of the menstrual cycle remains relatively constant throughout the reproductive years, but as a woman approaches menopause the cycle gradually shortens. Although blood loss is difficult to quantify, most loss occurs in the first few days of menses, and bleeding generally lasts from 2 to 7 days. The cycle length and the volume and duration of bleeding remain fairly constant for a woman throughout her reproductive years. After menopause, bleeding ceases completely. Abnormal vaginal bleeding may include noncyclic, excessive, or prolonged bleeding in the premenopausal patient or any vaginal bleeding in the postmenopausal patient. Differential considerations vary with patient age, hormonal status, and risk factors for endometrial carcinoma. The perimenopausal patient with abnormal bleeding is a special clinical challenge since menstrual bleeding is less predictable in this age group. Vaginal bleeding may occasionally be misinterpreted as hematuria. The latter should be excluded by clinical history, catheterized urine specimen, and/or physical examination.

Endometrial carcinoma is the most common gynecologic cancer in the United States, with a mean age of 60 years at diagnosis. Although 20% of cases are diagnosed in premenopausal women, most patients are postmenopausal. The most common presentation is abnormal vaginal bleeding, a finding that is seen in over 90% of postmenopausal women with endometrial carcinoma. However, even in the postmenopausal patient, endometrial cancer accounts for only up to 10% of uterine bleeding, with endometrial atrophy being the most common etiology in 50% of the cases. Only about 15% of cancers occur in women without bleeding. The early diagnosis of endometrial carcinoma allows for the best opportunity for cure. Therefore, endometrial carcinoma should be rigorously excluded in any postmenopausal or perimenopausal patient with abnormal bleeding and in younger patients with significant risk factors, such as obesity and anovulation. Anovulatory bleeding is the most common etiology of abnormal bleeding in the premenopausal patient. However, anatomic abnormalities such as endometrial and cervical polyps and submucosal fibroids may also be a cause and are found in up to 40% of premenopausal patients evaluated for this symptom. Other abnormalities that may cause abnormal bleeding include endometrial hyperplasia, fibroids, adenomyosis, cervical and vaginal neoplasia, and other less common uterine tumors and coagulopathies (most commonly Von Willebrand disease). Pregnancy-related complications should always be excluded in any woman of reproductive age with abnormal bleeding.

In the nonpregnant premenopausal patient without risk factors for endometrial carcinoma, a trial of medical therapy may initially be undertaken if anovulatory cycles are suspected. In the postmenopausal patient or if bleeding persists despite medical therapy in the premenopausal patient, endometrial sampling or imaging is warranted. Although imaging procedures cannot replace definitive histologic diagnosis, they play an important role in screening, further characterizing anatomic abnormalities, and directing appropriate patient care, often preventing unnecessary diagnostic procedures. For further evaluation of the patient with inconclusive biopsy results or persistent bleeding despite negative biopsy findings, imaging can be essential.

In the setting of abnormal vaginal bleeding, office endometrial sampling now has largely replaced dilatation and curettage (D&C); however, issues of access to the endometrial cavity and sampling error limit the clinical value of a negative result. Furthermore, only about 60% of the endometrial cavity is curetted with D&C, and many focal lesions may be missed, making the detection of focal structural causes for bleeding a vital role of imaging in this clinical setting. One prospective study evaluated 105 postmenopausal women presenting with vaginal bleeding. Patients underwent

D&C followed by hysteroscopic examination. Ninety-eight percent of women were found to have a focal growth pattern at hysteroscopy and of those D&C failed to diagnose 58% of polyps, 50% of hyperplasia, 60% of atypical hyperplasia, and 11% of endometrial cancers. In a retrospective study evaluating 311 women with abnormal vaginal bleeding, D&C failed to detect intrauterine disorders in 52.7% of patients who were subsequently diagnosed at hysterectomy.

Transvaginal Ultrasound

Transvaginal ultrasound (TVUS) is generally the initial imaging procedure of choice for evaluating abnormal vaginal bleeding due to its high sensitivity for depiction of endometrial pathology, its widespread availability, and its excellent safety profile and cost-effectiveness. In the postmenopausal patient, endometrial thickness is a well-established predictor of endometrial disease, and TVUS is the mainstay in detecting and characterizing abnormal endometrial thickening with highly reproducible measurements. Endometrial thickness refers to the double thickness measurement (sum of the thickness of the two endometrial layers excluding any intracavitary fluid). In order to obtain accurate endometrial measurements, it is crucial to perform the TVUS on days 4 to 10 of the menstrual cycle after the endometrium is sloughed in premenopausal women. For postmenopausal women on hormone replacement therapy (HRT), imaging is time-sensitive and will depend on the type of hormonal regimen (continuous combined versus cyclic hormones). If an abnormally thickened endometrium is identified, nonfocal endometrial biopsy is generally advocated as the next diagnostic step to exclude diffuse endometrial pathology, including carcinoma and hyperplasia. Alternatively, saline infusion sonohysterography (SIS) may be obtained to differentiate between focal and diffuse abnormalities and to guide hysteroscopic biopsy.

In a meta-analysis of 35 studies including 5,892 postmenopausal women, using 5 mm as the upper threshold for normal endometrial thickness, the sensitivity of TVUS for detecting endometrial cancer was 96%. An endometrial thickness of ≤5 mm was associated with a less than 1% probability of endometrial cancer. Sensitivity for the detection of cancer did not differ for women taking HRT compared to those not taking HRT. Many additional studies have further demonstrated that with an endometrial thickness of <5 mm, the risk of endometrial cancer is very low. An expert panel for the evaluation of postmenopausal bleeding concluded that if US shows a normal-appearing endometrium with a double thickness measurement of ≤5 mm, the test can be considered negative for endometrial carcinoma. A similar criterion can be used for women taking HRT, tamoxifen, or other selective estrogen receptor modulator therapy. Recent guidelines from the American College of Obstetrics and Gynecology advocate using 4 mm as the endometrial thickness cutoff that reasonably excludes endometrial carcinoma. However, this threshold may be associated with lower specificity and more false-positive US examinations.

In the asymptomatic postmenopausal patient without bleeding, the use of TVUS for screening is controversial. There is lack of consensus regarding what endometrial thickness best separates those with from those without endometrial pathology, and further validation is necessary. Upper threshold values ranging from 4 mm to 11 mm have been suggested. In addition to endometrial thickness, individual patient parameters such as age, hormonal therapy, and other risk factors for endometrial carcinoma must also be considered in patient management decisions.

The value of endometrial thickness as an indicator for endometrial pathology in the premenopausal patient is unreliable, as it may vary widely depending on phase of menstrual cycle. The optimum threshold level of endometrial thickness that should prompt further evaluation in this age group remains the subject of debate. The examination should ideally be performed during the early proliferative phase of the menstrual cycle when the endometrium is at its thinnest. A thickness >16 mm in a symptomatic premenopausal patient may be considered abnormal but with suboptimal sensitivity (67%) and specificity (75%). A recent study suggests that an endometrial thickness of 8 mm yields a higher sensitivity of 83.6% but with lower specificity of 56.4%. Focal heterogeneity or eccentric thickening of the endometrium detected at TVUS should always be further investigated regardless of endometrial thickness to exclude endometrial pathology. TVUS can help to identify focal lesions within the endometrium such as polyps and submucosal fibroids which may lead to sampling error and a negative biopsy result.

Abnormalities within the myometrium such as fibroids and adenomyosis may also be a cause of abnormal vaginal bleeding. Fibroids are readily demonstrated at sonography and can be characterized as submucosal, intramural, subserosal, or cervical in location. In a meta-analysis of 14 studies including 1,898 women who had US for uterine pathology, the pooled sensitivity and specificity for TVUS for the diagnosis of adenomyosis were 82.5% and 84.6%, respectively. However, detection of adenomyosis at TVUS may be limited if there is coexisting uterine pathology, such as fibroids. In one study, the sensitivity and specificity of TVUS for diagnosing adenomyosis in patients with and without fibroids were 33.3% and 78% and 97.8% and 97.1%, respectively.

Saline Infusion Sonohysterography

SIS (also referred to as sonohysterography or hysterosonography) consists of the instillation of sterile saline into the uterine cavity via a small catheter under TVUS guidance. This allows for better delineation of the endometrial lining when it is not clearly delineated on TVUS, which may occur in 5% to 10% of patients. This technique also allows for differentiation of focal lesions such as polyps from diffuse abnormalities such as endometrial hyperplasia. More recently, the use of gel instead of saline to fill the uterine cavity (gel-instillation sonography [GIS]) has shown some promising results, with sensitivity of 77.8% and 85% and specificity of 80.7% and 85% for SIS and GIS, respectively, for detecting intracavitary lesions. Because of its higher viscosity, a smaller amount of gel is required to adequately distend the uterine cavity, resulting in less patient

discomfort/pain and better technical results. As an advantage, this technique does not affect power Doppler signal in women with endometrial polyps, a phenomenon that had been reported previously when using saline.

Conventional two-dimensional (2-D) SIS and hysteroscopy show similar performance characteristics, with sensitivity of 95% to 96% and specificity of 88% to 90% for detecting/characterizing focal endometrial abnormalities. However, hysteroscopy allows for directed tissue sampling. SIS before hysteroscopy permits identification of a focal mass, prompting triage to a hysteroscopically directed biopsy procedure. SIS may also be used to further evaluate the endometrium in patients with negative TVUS and biopsy with persistent bleeding, allowing for detection of small intracavitary abnormalities, such as polyps or focal hyperplasia, not detectable by TVUS. In one study the sensitivity and specificity of SIS were 97.7% and 82.4%, respectively versus 83.0% and 70.6%, respectively for TVUS for detection of endometrial abnormalities such as polyps, submucosal fibroids, and endometrial hyperplasia in patients with abnormal vaginal bleeding. Differentiation of endometrial from subendometrial abnormalities, particularly in patients treated with tamoxifen, is also an important role for this technique with significant implications for patient management. Some investigators have compared the diagnostic accuracy of three-dimensional (3-D) SIS and that of conventional SIS. Although the 2 methods may show comparable or slightly higher sensitivity and specificity in diagnosing intrauterine lesions, 3-D SIS correlates better with hysteroscopy findings in premenopausal and postmenopausal patients with abnormal vaginal bleeding.

Transabdominal Ultrasound

Transabdominal pelvic US is usually performed in conjunction with TVUS, and the two techniques are complementary. Transabdominal scanning offers a wider field of view, increased depth of penetration, and an ability to evaluate adjacent organs. A transabdominal approach is particularly helpful for evaluating a markedly enlarged fibroid uterus, especially if there is extension of subserosal or pedunculated fibroids out of the pelvis. However, optimum evaluation of the endometrium generally requires TVUS, which allows for higher-resolution imaging. If the transvaginal probe cannot be tolerated, as is often the case in a prepubertal or virginal patient, transabdominal US using the urinary bladder as an acoustic window becomes essential.

Doppler Ultrasound

Color and pulsed Doppler US allow for the assessment of uterine and endometrial vascularization and may be of added value in further characterizing an endometrial abnormality detected at TVUS. Demonstration of blood flow in an intracavitary lesion excludes the possibility of a retained blood clot. Endometrial polyps often demonstrate a feeding vessel, which can aid in detection at TVUS. A recent study compared the mapping characteristics of power Doppler for the diagnosis of endometrial polyps versus submucosal fibroids. The authors found that the single vessel pattern had a sensitivity and specificity of 81.2% and 88.2%, respectively, for the diagnosis of endometrial polyps, whereas the rim-like pattern had a sensitivity and specificity of 70.6% and 100%, respectively, for the diagnosis of submucosal fibroids. However, the clinical usefulness of using intratumoral resistive indices and Doppler velocimetry of the uterine arteries in distinguishing benign from malignant processes remains under investigation.

Three-Dimensional Sonography

3-D sonography can be a useful adjunct to TVUS and SIS in the characterization of abnormalities within the endometrial cavity, including localization of focal abnormalities prior to directed biopsy. It allows the ability to reconstruct any plane of section, in orientations that cannot be obtained directly using standard 2-D sonography and SIS. In one study 3-D coronal view of the uterus was of added value to the standard 2-D pelvic sonogram in 24% of all patients referred for gynecologic sonography and in up to 39% of patients with an endometrial thickness $\geq$5 mm. Recently, 3-D power Doppler angiography combined with 3-D TVUS has become a new diagnostic tool to evaluate vascular patterns in the abnormal endometrium and endometrial volume. Although some advocate its potential usefulness in allowing for differentiation between benign and malignant causes of a thickened endometrium, others do not find it superior to the diagnostic capabilities of 2-D US.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the pelvis may be a useful problem-solving tool when US findings are not definitive. Uterine anatomy is well-delineated at MRI secondary to inherent soft-tissue contrast of uterine tissues. Although not a first-line test, MRI may be considered for evaluating the endometrium when TVUS is not possible or when the endometrium cannot be well visualized due to uterine orientation or coexisting abnormalities such as adenomyosis or leiomyomas. MRI may provide additional important information regarding fibroid number, size, and location prior to intervention such as embolization or myomectomy. MRI may also help to confirm the diagnosis of adenomyosis, which may be difficult at TVUS when there are coexisting fibroids. In a recent study evaluating the diagnostic performance of MRI in the detection for adenomyosis and fibroids, MRI had a positive predictive value of 92.3% and 95.7%, respectively.

In a woman with an enlarging or an abnormally enlarged uterus where underlying malignancy is a concern and US does not delineate the endometrium, MRI may assist in identification of a thickened endometrial lining or of morphological lesions such as fibroids or adenomyosis. Although MRI-detected features of benign endometrial polyps overlap with those of carcinoma, most polyps are benign. The prevalence of

malignancy in endometrial polyps increases with patient age but is generally less than 3% in postmenopausal patients and less than 1% in women of childbearing age. Histologic confirmation remains necessary when an endometrial mass is identified at MRI. However, evidence of an endometrial lesion invading the myometrium is suggestive of malignancy. In a recent study assessing the diagnostic accuracy of MRI in local staging of endometrial carcinoma, contrast-enhanced MRI showed a 90% sensitivity and 80% specificity for evaluating deep myometrial invasion. Also, demonstration of enhancement of an intracavitary abnormality with gadolinium contrast agents confirms the presence of a mass and excludes the possibility of a retained blood clot or debris. Results of initial studies investigating the added value of diffusion-weighted imaging in differentiating benign from malignant endometrial lesions show promise, but further investigation is necessary before this technique can be applied to clinical practice. A recent prospective study showed that apparent diffusion coefficient (ADC) values were significantly lower in endometrial cancers compared to those of normal endometrium and normal myometrium. The investigators, however, concluded that there was no correlation between ADC values and depth of myometrial invasion, histologic tumor grading, and presence of metastatic lymphadenopathy.

Computed Tomography

Computed tomography (CT) is generally not warranted for evaluating vaginal bleeding since uterine anatomy is not well characterized due to limited soft-tissue contrast resolution. For detection of endometrial thickening using TVUS as the reference standard, the sensitivity, specificity, and positive and negative predictive values of multidetector CT were 53.1%, 93.5%, 66.7%, and 89.1%, respectively, in one recent study. Multiplanar reformation may be a helpful addition to standard axial images when evaluating the endometrium at multidetector CT, with reconstructed images in the sagittal plane being particularly useful in determining the degree of myometrial invasion in patients with endometrial carcinoma. However, an abnormal endometrium incidentally detected at CT should be referred to TVUS for further evaluation.

Positron Emission Tomography/Computed Tomography

Positron emission tomography (PET) with CT (PET/CT) is not warranted for evaluating vaginal bleeding. In premenopausal patients, normal endometrial uptake of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) changes cyclically, increasing during the ovulatory and menstrual phases. This variation requires that the evaluation of the endometrium be correlated with the menstrual history. In postmenopausal women, increased tracer uptake is considered abnormal. Neither use of contraceptives nor hormonal therapy is associated with a significant increase in endometrial tracer uptake. Abnormal endometrial tracer uptake incidentally detected on PET should be referred for TVUS evaluation.

Summary

- Imaging can play an important role in screening, characterization of structural abnormalities, and directing appropriate patient care, often preventing inappropriate diagnostic procedures. However, imaging procedures cannot replace definitive histologic diagnosis.
- TVUS is generally the initial imaging procedure of choice for evaluating abnormal vaginal bleeding, and endometrial thickness is a well-established predictor of endometrial disease in postmenopausal women. Endometrial thickness measurements of ≤5 mm and ≤4 mm have been advocated as appropriate threshold values to reasonably exclude endometrial carcinoma in the postmenopausal age group. However, the most appropriate value for upper limits normal for the asymptomatic postmenopausal patient without bleeding remains the subject of debate. An upper threshold value of 16 mm has been suggested for the premenopausal patient with abnormal bleeding, although it remains controversial as endometrial thickness varies greatly in this patient age group.
- Transabdominal US is generally an adjunct to TVUS and is most helpful when TVUS cannot be performed or when there is poor visualization of the endometrium secondary to uterine position or poor penetration due to associated uterine pathology such as fibroids or adenomyosis.
- Tissue sampling may be the most appropriate initial step in the evaluation of abnormal vaginal bleeding.
- SIS after TVUS allows for identification of focal abnormalities within the endometrial cavity, which may then guide hysteroscopic biopsy or resection. GIS may represent an adequate substitute to SIS in the future.
- Color and duplex Doppler allow for assessment of uterine and endometrial vascularization and may be of added value in further characterizing an endometrial abnormality detected at TVUS. Endometrial polyps will often have a feeding vessel, which aids in their detection.
- Pelvic MRI is an important problem-solving tool and adjunct to TVUS, particularly when SIS cannot be performed for technical reasons or to better define extent of disease if endometrial carcinoma is suspected. Adding diffusion-weighted sequences may improve preoperative assessment of patients with endometrial carcinoma.
- CT is generally not warranted for evaluating a patient with abnormal vaginal bleeding. An abnormal endometrium incidentally detected at CT should be referred to TVUS for further evaluation.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based

contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 m^2), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Abbreviations

- 2-D, two-dimensional
- 3-D, three-dimensional
- CT, computed tomography
- MRI, magnetic resonance imaging
- SIS, saline infusion sonohysterography
- TVUS, transvaginal ultrasound
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Abnormal vaginal bleeding

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Family Practice

Internal Medicine

Obstetrics and Gynecology

Pathology

Radiology

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of initial radiologic examinations for patients with abnormal vaginal bleeding

Target Population

Women with abnormal vaginal bleeding

Interventions and Practices Considered

1. Ultrasound (US)
    - Pelvis transvaginal
    - Pelvis transabdominal
    - Saline infusion sonohysterography (SIS)
    - Duplex Doppler pelvis
2. Computed tomography (CT) pelvis
    - With contrast
    - Without contrast
    - Without and with contrast
3. Magnetic resonance imaging (MRI) pelvis
    - Without and with contrast
    - Without contrast

Major Outcomes Considered

- Utility of radiologic examinations in differential diagnosis
- Sensitivity, specificity, accuracy, and positive/negative predictive value of radiologic examinations

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Study Quality Category Definitions

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - There are important study design limitations.

Category 4 - The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:

a. The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description).
b. The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence.
c. The study is an expert opinion or consensus document.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed a published cost analysis.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiologic imaging procedures for patients with abnormal vaginal bleeding

Potential Harms

Gadolinium-based Contrast Agents

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 m^2), and almost never in other patients. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Relative Radiation Level

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Khati NJ, Glanc P, Bhosale PR, Harisinghani MG, Harris RD, Kim YB, Mitchell DG, Nyberg DA, Pandharipande PV, Pannu HK, Shipp TD, Siegel CL, Simpson L, Wall DJ, Wong-You-Cheong JJ, Zelop CM, Javitt MC, Expert Panel on Women's Imaging. ACR Appropriateness CriteriaÂ® abnormal vaginal bleeding [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 13 p. [63 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1996 (revised 2014)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Bennett GL, Andreotti RF, Lee SI, Allison SO, Brown DL, Dubinsky T, Glanc P, Mitchell DG, Podrasky AE, Shipp TD, Siegel CL, Wong-You-Cheong JJ, Zelop CM, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® abnormal vaginal bleeding. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p. [59 references]

Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 90 p. Electronic copies: Available from the ACR Web site.

- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available from the ACR Web site .
- ACR Appropriateness Criteria® abnormal vaginal bleeding. Evidence table. Reston (VA): American College of Radiology; 2014. 22 p. Electronic copies: Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on August 25, 2006. This NGC summary was updated by ECRI Institute on August 10, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on July 29, 2011 and August 14, 2014.

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